AMENDMENTS TO THE DRAWINGS

Please replace Figure 22 with the Replacement Sheet for Figure 22.

Please replace Figure 25D with the Replacement Sheet for Figure 25D.

REMARKS

1. Formal Matters

a. Status of the Claims

Claims 1-24 are pending in this application. Claims 1-24 are hereby canceled without prejudice to pursuing these claims in a continuing application. Claims 25-33 are new. Upon entry of these amendments, claims 25-33 are pending and under active consideration. Applicants respectfully request entry of the amendments and remarks made herein into the file history of the present application.

b. Amendments to the Claims

New claim 25 recites a nucleic acid consisting of X nucleotides wherein X is 16-120, support for which may be found at paragraph 0038 of the application as originally filed. New claim 25 also recites that the sequence of the nucleic acid may comprise at least 16 consecutive nucleotides of SEQ ID NO: 10068310, support for which may be found at Table 10 of the application as originally filed. Table 10, lines 345905-345934 recites:

> The GR5737 folded precursor RNA, herein designated GR FOLDED PRECURSOR RNA is naturally processed by cellular enzymatic activity into at least 82 separate GAM precursor RNAs GAM353392 precursor RNA, GAM353393 precursor RNA, GAM353394 precursor RNA, GAM353395 precursor RNA, GAM353396 precursor RNA, GAM353397 precursor RNA, GAM463777 precursor RNA, GAM353398 precursor RNA, GAM353399 precursor RNA, GAM353400 precursor RNA, GAM353401 precursor RNA, GAM353402 precursor RNA, GAM353403 precursor RNA, GAM353404 precursor RNA, GAM353405 precursor RNA, GAM353406 precursor RNA, GAM353407 precursor RNA, GAM353408 precursor RNA, GAM353409 precursor RNA, GAM340661 precursor RNA, GAM353410 precursor RNA, GAM353411 precursor RNA, GAM353412 precursor RNA, GAM353413 precursor RNA, GAM353414 precursor RNA, GAM463778 precursor RNA, GAM415273 precursor RNA, GAM435659 precursor RNA, GAM435660 precursor RNA, GAM415274 precursor RNA, GAM415275 precursor RNA, GAM353415 precursor RNA, GAM353416 precursor RNA, GAM399339 precursor RNA, GAM353417 precursor RNA, GAM353418 precursor RNA, GAM353419 precursor RNA, GAM353420 precursor RNA, GAM353421 precursor RNA, GAM353422 precursor RNA, GAM353423 precursor RNA, GAM353424 precursor RNA,

GAM353425 precursor RNA, GAM353426 precursor RNA, GAM353427 precursor RNA, GAM353428 precursor RNA, GAM353429 precursor RNA, GAM353430 precursor RNA, GAM353431 precursor RNA, GAM353432 precursor RNA, GAM463780 precursor RNA, GAM353433 precursor RNA, GAM353434 precursor RNA, GAM353435 precursor RNA, GAM353436 precursor RNA, GAM353437 precursor RNA, GAM353438 precursor RNA, GAM353439 precursor RNA, GAM353440 precursor RNA, GAM353441 precursor RNA, GAM353442 precursor RNA, GAM353443 precursor RNA, GAM353444 precursor RNA, GAM353445 precursor RNA, GAM353446 precursor RNA, GAM353447 precursor RNA, GAM353448 precursor RNA, GAM353449 precursor RNA, GAM353450 precursor RNA, GAM353451 precursor RNA, GAM353452 precursor RNA, GAM399341 precursor RNA, GAM353453 precursor RNA, GAM353454 precursor RNA, GAM353455 precursor RNA, GAM353456 precursor RNA, GAM353457 precursor RNA, GAM353458 precursor RNA, GAM353459 precursor RNA, GAM353460 precursor RNA, GAM353461 precursor RNA and GAM353462 precursor RNA, herein schematically represented by GAM1 FOLDED PRECURSOR RNA through GAM3 FOLDED PRECURSOR RNA. Each GAM folded precursor RNA is a hairpin-shaped RNA segment, corresponding to GAM FOLDED PRECURSOR RNA of Fig. 8.

As shown in Table 1 below, the following SEQ ID NOS, all of which were disclosed in the application as originally filed, represent the sequences of the following GAMS, which are all products of the processing of GR5737 (SEQ ID NO: 10068310):

Table 1

SEQ ID NO	GAM	Genomic positions from chromosome 14, plus strand (according to Human Genome Sequence hg 18, NCBI Build 36.1, March 2006)
6876154	353396	100558142 - 100558228
6852582	353399	100561081 - 100561193
6792146	353405	100562873 - 100562957
6866677	353406	100563193 - 100563275
6816665	353410	100565724 - 100565805
6807279	415273	100576159 - 100576245
6766934	435659	100576864 - 100576950
6764600	415274	100582536 - 100582618
6846774	415275	100583402 - 100583490
6759618	353416	100584748 - 100584839
6797277	399339	100585662 - 100585742
6859396	353422	100588529 - 100588609
6862412	353424	100590396 - 100590478
6758196	353432	100591348 - 100591414
6767976	463780	100591501 - 100591582
6864591	353446	100596663 - 100596765
6846490	353450	100598122 - 100598210
6827549	353455	100601368 - 100601495
6824457	353456	100601543 - 100601624
6832127	353457	100601684 - 100601763
6773276	353459	100602007 - 100602078
6791269	353462	100602810 - 100602890

The GAMS of Table 1 are located on the plus strand of human chromosome 14 as indicated in Table 1. Therefore, SEQ ID NO: 10068310 (GR5737) represents the sequence of the GAMS listed in Table and the intervening sequences that are located in between the GAMS of Table 1 at the following genomic locations:

Table 2

Genome positions of intervening sequences on chromosome 14, plus strand
100558229-100561080
100561194-100562872
100562958-100563192
100563276-100565723
100565806-100576158
100576246-100576863
100576951-100582535
100582619-100583401
100583491-100584747
100584840-100585661
100585743-100588528
100588610-100590395
100590479-100591347
100591415-100591500
100591583100596662
100596766100598121
100598211-100601367
100601496-100601542
100601625-100601683
100601764-100602006
100602079-100602809

SEQ ID NO: 10068310 (GR5737) thus in total represents the plus strand of human chromosome 14 at positions 100558142 to 100602890 (See Table 1).

New claim 25 also recites that the nucleic acid may be an RNA equivalent of (a), support for which may be found at paragraph 0036 of the application as originally filed.

New claim 25 is further directed to a nucleic acid that may be: a sequence at least 80% identical to (a) or (b), support for which may be found at paragraph 0046 and claim 1 of the application as originally filed.

New claim 25 further recites that the nucleic acid may be: the complement of any one of (a)-(c), support for which may be found at paragraph 0036 of the application as originally filed.

New claim 26 is directed to the nucleic acid of claim 25, wherein the at least Y nucleotides is of a sequence selected from the group consisting of SEQ ID NOS: 6876154,

6852582, 6792146, 6866677, 6816665, 6807279, 6766934, 6764600, 6846774, 6759618, 6797277, 6859396, 6862412, 6758196, 6767976, 6864591, 6846490, 6827549, 6824457, 6832127, 6773276, and 6791269, support for which can be found at the sequence listing as originally filed.

New claim 27 recites the nucleic acid of claim 25, wherein the at least Y nucleotides is of a sequence selected from the group consisting of SEQ ID NOS: 4819, 4843, 2249, 488, 488, 1199, 7002375, 6946165, 6907159, 6907159, 6971545, 7012403, 6772, 6910855, 6982884, 3106, 3343, 1454, 2802, 3307, 6939857, 6939857, 507, 3676, 1406, 1406, 6413, 1330, 2877, 4542, 8145, 5874, and 468, support for which can be found at the sequence listing as originally filed.

New claim 28 is directed to a nucleic acid of claim 25, wherein X=Y, support for which can be found at claim 25 as described above.

New claim 29 recites the nucleic acid of claim 28, wherein Y consecutive nucleotides is of a sequence selected from the group consisting of SEQ ID NOS: 6876154, 6852582, 6792146, 6866677, 6816665, 6807279, 6766934, 6764600, 6846774, 6759618, 6797277, 6859396, 6862412, 6758196, 6767976, 6864591, 6846490, 6827549, 6824457, 6832127, 6773276, and 6791269, support for which can be found at the sequence listing as originally filed.

New claim 30 is directed to the nucleic acid of claim 28, wherein Y consecutive nucleotides is of a sequence selected from the group consisting of SEQ ID NOS: 4819, 4843, 2249, 488, 488, 1199, 7002375, 6946165, 6907159, 6907159, 6971545, 7012403, 6772, 6910855, 6982884, 3106, 3343, 1454, 2802, 3307, 6939857, 6939857, 507, 3676, 1406, 1406, 6413, 1330, 2877, 4542, 8145, 5874, and 468, support for which can be found at the sequence listing as originally filed.

New claim 31 recites a vector comprising an insert, wherein an insert consists of the nucleic acid of claim 25, support for which can be found at paragraph 0026 of the application as filed.

New claim 32 is directed to a vector comprising an insert, wherein an insert consists of the nucleic acid of claim 28, support for which can be found at paragraph 0026 of the application as filed.

New claim 33 a method for detecting the nucleic acid of claim 27, comprising providing a biological sample and measuring the level of the nucleic acid, wherein a difference in the level

of the nucleic acid compared to a control is indicative of the presence of the nucleic acid, support for which can be found at paragraph 0230 and claim 19 of the application as originally filed.

c. Amendments to the Specification

Paragraph 0263 is amended to assign SEQ ID NOS: 10068286-10068296 to the sequences shown in Fig. 23A in compliance with 37 C.F.R. §§ 1.821-1.825.

Paragraph 0266 is amended to assign SEQ ID NOS: 10068281-10068285 to the sequences shown in Fig. 24A in compliance with 37 C.F.R. §§ 1.821-1.825.

Paragraph 0499 is amended to assign SEQ ID NOS: 10068178-10068183 to the listed sequences in compliance with 37 C.F.R. §§ 1.821-1.825.

Paragraphs 0562-0582 are amended to assign SEQ ID NOS: 10068186-10068189, 10068192-10068193, and 10068306-10068309 to the listed sequences in compliance with 37 C.F.R. §§ 1.821-1.825.

d. Amendments to the Drawings

Figure 22 is amended by replacing it with a Replacement Sheet for Fig. 22 to assign SEQ ID NOS: 10068194-10068280 to the listed sequences in compliance with 37 C.F.R. §§ 1.821-1.825.

Figure 25D is amended by replacing it with a Replacement Sheet for Fig. 25D to assign SEQ ID NOS: 10068297-10068305 to the listed sequences in compliance with 37 C.F.R. §§ 1.821-1.825. No new matter has been added.

e. Notice to Comply with Sequence Rules

On page 2 of the Office Action, the Examiner alleges that the specification and sequence listing do not comply with 37 C.F.R. §§ 1.821-1.825. Specifically, the Examiner alleges that sequence identifiers are not associated with sequences disclosed in Figures 22, 23, 24, and 25, and paragraphs 0499, and 0559-0582.

Applicant submits herewith a replacement sequence listing pursuant to 37 C.F.R. § 1.825(a), and the specification and drawings are amended throughout to disclose the appropriate SEQ ID NOS in accordance with 37 C.F.R. §§ 1.821-1.825. No new matter has been added.

In light of the amendments to the specification described hereinabove, and the replacement drawings and replacement sequence listing submitted herewith, Applicant respectfully submits that the application is in compliance with 37 C.F.R. §§ 1.821-1.825.

f. Election/Restrictions

On pages 3-6 of the Office Action, the Examiner requires restriction to one of the following inventions under 35 U.S.C. § 121:

I. Claims 1-11 and 20-23, drawn to a bioinformatically detectable isolated oligonucleotide, which anneals to a portion of a mRNA transcript of target gene, and which modulates or represses expression of said target gene.

II. Claims 12, 16, and 17, drawn to a method of treatment of a disease, comprising providing a material that modulates or inhibits the activity of a microRNA, and to methods thereof wherein the material is an oligonucleotide.

III. Claims 13-15, drawn to a method for treatment of a disease, comprising providing a material that binds a segment of a mRNA and inhibits the expression of protein from said mRNA, and to methods thereof wherein the material is a microRNA.

IV. Claims 18 and 19, drawn to a method for diagnosis of a disease, comprising assaying a microRNA, and to a method for detection of expression of an oligonucleotide.

V. Claim 24, drawn to a method for bioinformatic detection of microRNA.

Applicant elects without traverse Group I, which now is considered claims 25-33, drawn to an isolated nucleic acid, a vector comprising the nucleic acid, and a method for detecting the nucleic acid.

g. Restriction to a Single Nucleotide Sequence and mRNA target gene

On pages 6-8 of the Office Action, the Examiner requires restriction to a single nucleic acid sequence for the elected Group I under 35 U.S.C. § 121. Applicant elects with traverse nucleic acids related to SEQ ID NO: 10068310, which is associated with claims 25-33 for further prosecution.

The Examiner is permitted under 35 U.S.C. § 121 to issue a restriction requirement between independent and distinct inventions. However, the Director has partially waived the requirements of 37 C.F.R. § 1.141 *et seq.* to permit a reasonable number of nucleotide sequences to be claimed in a single application. *See* Examination of Patent Applications Containing Nucleotide Sequence, 1192 O.G. 68 (November 19, 1996). It has been determined that normally

ten sequences constitute a reasonable number for examination purposes absent an exceptional case. *See* MPEP 803.04.

The Examiner has failed to demonstrate that the claimed sequences are an exceptional case necessitating that the number of sequences to be selected be less than ten. Applicant respectfully submits that the Examiner is impermissibly disregarding the waiver of 37 C.F.R. § 1.141 *et seq*. Accordingly, Applicant respectfully requests reconsideration of the restriction requirement and the opportunity to elect up to ten sequences for further prosecution.

h. Species Election Regarding Target Genes in Group I

On page 8 of the Office Action, the Examiner requires election of a single disclosed target gene species for Group I under 35 U.S.C. § 121. Applicant elects without traverse the target gene MAP2K4 , which has the sequence SEQ ID NO: 3010.

2. Conclusion

Applicant respectfully submits this application is in good and proper order for substantive examination.

Respectfully submitted,

POLSINELLI SHALTON FLANIGAN SUELTHAUS PC

Dated: March 21, 2007

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